

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Stephen R. Hanson
Serial No: Not yet assigned
Conf. No; Not yet assigned
Filed: Herewith
For: METHODS AND COMPOSITIONS FOR TREATING PLATELET-
RELATED DISORDERS USING MPL PATHWAY INHIBITORY
AGENTS
Examiner: Not yet assigned
Art Unit: Not yet assigned

Mail Stop Patent Application

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the
Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed within three months of the filing
of the application and before the mailing date of a first Office Action on the merits in the
above-identified case.

No fee or certification is required.

PART II: Information Cited

The Applicant hereby makes of record in the above-identified application the
information listed on the attached form PTO-1449 (modified). The order of presentation of
the references should not be construed as an indication of the importance of the references.

The Applicant hereby makes the following additional information of record in the
above-identified application:

International Search Report for PCT/US00/25781, filed September 21, 2000 (copy enclosed)
International Search Report for PCT/US00/26025, filed September 21, 2000 (copy enclosed)

591699.1

The Applicant would like to bring to the Examiner's attention the following co-pending application (copy enclosed):

<u>Docket No.</u>	<u>Serial No.</u>	<u>Filing Date</u>	<u>Title of Application</u>
E0355/7004	09/666,223	09/21/2000	Methods and Compositions for Treating Platelet-Related Disorders

PART III: Explanation of Non-English Language References and Remarks Concerning Other Information Cited

The following is a concise explanation of the relevance of each non-English language reference listed on the attached form PTO-1449 (modified):

The following are remarks concerning the other information cited:

PART IV: Remarks

Documents cited on the attached form PTO-1449 (modified) are enclosed unless otherwise indicated on the attached form PTO-1449 (modified). It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

Serial No.: Not yet assigned

- 3 -

Art Unit: Not yet assigned

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,

By: 

Maria A. Trevisan, Reg No. 48,207
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210
Telephone (617) 720-3500

Docket No. E00355.70006.US

Dated: June 24, 2003
x6/31/03x

FORM PTO-1449/A and B (Modified) INFORMATION DISCLOSURE STATEMENT BY APPLICANT				APPLICATION NO.: Not yet assigned	ATTY. DOCKET NO.: E00355.70006.US
				FILING DATE: June <u>24</u> , 2003	
				APPLICANT: Stephen R. Hanson	
				GROUP ART UNIT: Not yet assigned	EXAMINER: Not yet assigned
Sheet	1	of	4		

U.S. PATENT DOCUMENTS

Examiner's Initials#	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYY
		Number	Kind Code		
	*A1	6,008,232		Lakshmanan	12/28/99
	*A2	5,789,539		Daly, et al.	08/04/98
	*A3	5,620,960		Arnold, et al.	04/15/97
	*A4	5,572,944		Gewirtz, et al.	12/05/95
	*A5	5,506,107		Cunningham, et al.	04/09/96
	*A6	5,440,020		Coller	08/08/95
	*A7	5,391,557		Cullinan, et al.	02/21/95
	*A8	5,306,709		Gewirtz	04/26/94
	*A9	5,185,323		Gewirtz	02/09/93
	*A10	4,847,276		Yarrington	07/11/89
	*A11	4,206,214		Harker, et al.	06/03/80
	*A12	4,146,718		Jenks, et al.	03/27/79
	*A13	4,088,753		Parmer	05/09/78
	*A14	3,932,407		Beverung, Jr., et al.	01/13/76
	*A15	RE31,617		Beverung, Jr., et al.	06/26/84
	*A16	5,830,647		Eaton, et al.	11/03/98
	*A17	5,756,083		Elliott	05/26/98
	*A18	5,932,546		Barrett, et al.	08/03/99
	*A19	5,869,451		Dower, et al.	02/09/99
	*A20	6,103,740		Lakshmanan	08/15/00
	*A21	5,498,599		Choi, et al.	03/12/96
	*A22	4,743,445		Delwiche, et al.	05/10/98
	*A23	6,150,120		Spivak et al.	11/21/00

FOREIGN PATENT DOCUMENTS

Examiner's Initials#	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/Country	Number	Kind Code			
	*B1	WO	97/28190			08/97	-
	*B2	WO	99/08524			02/99	-
	*B3	WO	99/08525			02/99	-
	*B4	EP	0 904 783			03/99	-
	*B5	WO	96/40750			12/96	
	*B6	WO	96/25498			08/96	
	*B7	WO	99/10494		Genentech, Inc.	04/99	

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials#	Cite No.	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
	*C1	Al-Jibouri, L.M. and Najim, R.A., "Effect of dipyridamole on blood glucose and liver cyclic AMP levels and platelet count during endotoxaemia in mice", <i>Clin. Exp. Pharmacol. Physiol.</i> , 15(7):527-32 (1988) ABSTRACT	

	*C2	Andes, et al., "Inhibition of platelet production induced by an antiplatelet drug, anagrelide, in normal volunteers", <i>Thromb Haemost.</i> , 52(3):325-8 (1984)	
	*C3	Balan, K.K and Critchley, M., "Outcome of 259 patients with primary proliferative polycythaemia (PPP) and idiopathic thrombocythaemia (IT) treated in a regional nuclear medicine department with phosphorus-32—a 15 year review", <i>Br. J. Radiol.</i> , 70(839):1169-73 (1997) ABSTRACT	
	*C4	Baldini, et al., "Effect of anagrelide on platelet count and function in patients with thrombocytosis and myeloproliferative disorders", <i>Haematologica</i> , 77(1):40-3 (1992) ABSTRACT	
	*C5	Barnathan, et al., "Aspirin and dipyridamole in the prevention of acute coronary thrombosis complicating coronary angioplasty", <i>Circulation</i> , 76(1):125-134 (1987)	
	*C6	Bellucci, et al., "Positive and negative regulation of megakaryocytopoiesis", <i>C.R. Seances Soc. Biol. Fil.</i> , 190(5-6):515-32 (1996) ABSTRACT	
	*C7	Bunn, H.F., "Pathophysiology of the anemias", <i>Harrison's Principles of Internal Medicine: Hematology and Oncology</i> , 1514, 1566-67 New York, McGraw-Hill, (1991)	
	*C8	Cazenave, J.P. and Gachet, C., "Anti-platelet drugs: do they affect megakaryocytes?", <i>Baillieres Clin Haematol</i> , 10(1):163-80 (1997)	
	*C9	Chen, et al., "Thrombospondin, a negative modulator of megakaryocytopoiesis", <i>J. Lab. Clin. Med.</i> , 129(2):231-8 (1997) ABSTRACT	
	*C10	Cortelazzo, et al., "Hydroxyurea for patients with essential thrombocythemia and a high risk of thrombosis", <i>N. Engl. J. Med.</i> , 332(17):1132-6 (1995) ABSTRACT	
	*C11	Dale, et al., "Chronic thrombocytopenia is induced in dogs by development of cross-reacting antibodies to the MpL ligand", <i>Blood</i> , 90(9):3456-3461 (1997)	
	*C12	Davies, et al., "Adverse events reported by postmenopausal women in controlled trials with raloxifene", <i>Obstetrics & Gynecology</i> , 93(4):558-565 (1999)	
	*C13	De Serres, et al., "Immunogenicity of thrombopoietin mimetic peptide GW395058 in BALB/c mice and New Zealand white rabbits: evaluation of the potential for thrombopoietin neutralizing antibody production in man", <i>Stem Cells</i> , 17:203-209 (1999)	
	*C14	Deng, et al., "A monoclonal antibody cross-reactive with human platelets, megakaryocytes, and common acute lymphocytic leukemia cells", <i>Blood</i> , 61(4):759-764 (1983)	
	*C15	Gaver, et al., "Disposition of anagrelide, an inhibitor of platelet aggregation", <i>Clin. Pharmacol. Ther.</i> , 29(3):381-6 (1981) ABSTRACT	
	*C16	Gewirtz, et al., "Cell-mediated suppression of megakaryocytopoiesis in acquired amegakaryocytic thrombocytopenic purpura", <i>Blood</i> , 68(3):619-26 (1986) ABSTRACT	
	*C17	Glushkov, et al., "Changes in hemostatic system indices during hemosorption in healthy dogs", <i>Biull Eksp Biol. Med.</i> , 94(7):95-8 (1982) ABSTRACT	
	*C18	Goldberg, et al., "Thrombocytotoxic suppression of megakaryocyte production from stem cells", <i>Blood</i> , 49(1):59-69 (1977) ABSTRACT	
	*C19	Gugliotta, et al., "In vivo and in vitro inhibitory effect of alpha-interferon on megakaryocyte colony growth in essential thrombocythaemia", <i>Br. J. Haematol.</i> , 71(2):177-81 (1989) ABSTRACT	
	*C20	Herron, et al., "Inhibition of megakaryocytic colonies <i>in vitro</i> by anagrelide", <i>Clin. Res.</i> , 34(2):459A (1986) ABSTRACT	
	*C21	Hung, et al., "Focused antithrombotic therapy: novel anti-platelet salicylates with reduced ulcerogenic potential and higher first-pass detoxification than aspirin in rats", <i>J. Lab. Clin. Med.</i> , 132(6):469-77 (1998) ABSTRACT	
	*C22	Jones, et al., "Inhibitors of cyclic AMP phosphodiesterase. 1. Analogues of cilostamide and anagrelide", <i>J. Med. Chem.</i> , 30(2):295-303 (1987) ABSTRACT	
	*C23	Lecomte-Raclet, et al., "New insights into the negative regulation of hematopoiesis by chemokine platelet factor 4 and related peptides", <i>Blood</i> , 91(8):2772-80 (1998) ABSTRACT	
	*C24	Ludwig, et al., "Interferon-alfa corrects thrombocytosis in patients with myeloproliferative disorders", <i>Cancer Immunol. Immunother.</i> , 25(3):266-73 (1987) ABSTRACT	
	*C25	Mazur, et al., "Analysis of the mechanism of anagrelide -induced thrombocytopenia in humans", <i>Blood</i> , 79(8):1931-1937 (1992)	
	*C26	Mazzucconi, et al., "Pipobroman therapy of essential thrombocythemia", <i>Scand J. Haematol.</i> , 37(4):306-9 (1986) ABSTRACT	
	*C27	Mazzucconi, et al., "Therapy with Anagrelide in patients affected by essential thrombocythemia: preliminary results", <i>Haematologica</i> , 77(4):315-7 (1992) ABSTRACT	
	*C28	McCune, et al., "Precipitous fall in platelet count with anagrelide: case report and critique of dosing recommendations", <i>Pharmacotherapy</i> , 17(4):822-6 (1997) ABSTRACT	
	*C29	Meanwell, et al., "Inhibitors of blood platelet cAMP phosphodiesterase. 2. Structure-activity relationships associated with 1,3-dihydro-2H-imidazo[4,5-b]quinolin-2-ones substituted with functionalized side chains", <i>J. Med. Chem.</i> , 35(14):2672-87 (1992) ABSTRACT	
	*C30	Nagae, S. and Hori, Y., "Immune thrombocytopenia due to Tranilast (Rizaben): detection of drug-dependent platelet-associated IgG", <i>J. Dermatol.</i> , 25(11):706-9 (1998)	
	*C31	Negrev, et al., "Influence of nonselective beta-adrenergic impacts on the effects of	

	thrombocytopoietin in mice", <i>Acta Physiologica et Pharmacologica Bulgaria</i> ", 13:1:35-39 (1987)	
*C32	Ramires, et al., "Effect of ticlopidine and dipyridamole on platelet aggregation and count in patients with chronic stable angina pectoris", <i>Arq Bras. Cardiol.</i> , 56(4):323-7 (1991) ABSTRACT	
*C33	Robak, T, et al., "Anagrelide—new antiplatelet drug", <i>Acta Haematol Pol.</i> , 25(4):309-15 (1994) ABSTRACT	
*C34	Sato, et al., "Multivariate analysis of risk factors for thrombus formation in University of Tokyo ventricular assist device", <i>J. Thorac. Cardiovasc. Surg.</i> , 106:520-7 (1993)	
*C35	Scott, et al., "Local delivery of an antithrombin inhibits platelet-dependent thrombosis", <i>Circulation</i> , 90(4):1951-1955 (1994)	
*C36	Seiler, et al., "Effects of anagrelide on platelet cAMP levels, cAMP-dependent protein kinase and thrombin-induced Ca++ fluxes", <i>J. Pharmacol Exp. Ther.</i> , 243(2):767-74 (1987) ABSTRACT	
*C37	Shinagawa, et al., "Allopurinol induced pancytopenia in a patient with myeloproliferative disorder", <i>Rinsho Ketsueki</i> , 38(1):64-71 (1997) ABSTRACT	
*C38	Smith, J.B. "Effect of thromboxane synthetase inhibitors on platelet function: enhancement by inhibition of phosphodiesterase", <i>Thromb Res.</i> , 15:28(4):477-85 (1982) ABSTRACT	
*C39	Solberg, et al., "The effects of anagrelide on human megakaryocytopoiesis", <i>Br. J. Haematol.</i> , 99(1):174-80 (1997) ABSTRACT	
*C40	Thaulow, et al., "Blood platelet count and function are related to total and cardiovascular death in apparently healthy men", <i>Circulation</i> 84(2):613-617 (1991)	
*C41	Trowbridge, et al., "Platelet production in myocardial infarction and sudden cardiac death", <i>Thromb. Haemost.</i> , 52(2):167-171 (1984)	
*C42	Van de Pette, "Primary thrombocythaemia treated with busulphan", <i>Br. J. Haematol.</i> , 62(2):229-37 (1986) ABSTRACT	
*C43	van der Loo, et al., "Megakaryocytes and platelets in vascular disease", <i>Bailliere's Clinical Haematology</i> , 10(1):109-123 (1997)	
*C44	Venuti, et al., "Inhibitors of cyclic AMP phosphodiesterase. 3. Synthesis and biological evaluation of pyrido and imidazolyl analogues of 1,2,3,5-tetrahydro-2-oxoimidazole[2,1-b]quinazoline", <i>J. Med. Chem.</i> , 31(11):2136-45 (1988) ABSTRACT	
*C45	Wada, et al., "Characterization of the truncated thrombopoietin variants", <i>Biochem. Biophys. Res. Comm.</i> , 213(3):1091-1098 (1995)	
*C46	Wadenvik, et al., "The effect of alpha-interferon on bone marrow megakaryocytes and platelet production rate in essential thrombocythemia", <i>Blood</i> , 77(10):2103-8 (1991) ABSTRACT	
*C47	Wilhelmsen, L., "Thrombocytes and coronary heart disease", <i>Circulation</i> 84(2):936-938 (1991)	
*C48	Yataganas, et al., "alpha Interferon treatment of essential thrombocythaemia and other myeloproliferative disorders with excessive thrombocytosis", <i>Eur. J. Cancer</i> , 27 Suppl 4:S69-71 (1991) ABSTRACT	
*C49	Yeager, et al., "Effects of cyclophosphamide on murine bone marrow and splenic megakaryocyte-CFC, granulocyte-macrophage-CFC, and peripheral blood cell levels", <i>J. Cell. Physiol.</i> , 112(2):222-8 (1982) ABSTRACT	
*C50	Harker, et al., "Regulation of Platelet Production and Function by Megakaryocyte Growth and Development Factor in Nonhuman Primates", <i>Blood</i> , Vol. 87, No. 5, pp. 1833-1844, (1996)	
*C51	Harker, "Platelets in Thrombotic Disorders: Quantitative and Qualitative Platelet Disorders Predisposing to Arterial Thrombosis", <i>Seminars in Hematology</i> , Vol. 35, No. 3, pp. 241-252, (1998)	
*C52	van der Loo, et al. " A Role for Changes in Platelet Production in the Cause of Acute Coronary Syndromes", <i>Arterioscler Thromb Vasc Biol.</i> , Vol. 19, pp. 672-679 (1999)	
*C53	Broudy, et al., "Thrombopoietin Stimulates Colony-Forming Unit-Megakaryocyte Proliferation and Megakaryocyte Maturation Independently of Cytokines that Signal through the gp130 Receptor Subunit," <i>Blood</i> , Vol. 8, No. 6, pp. 2026-2032 (1996)	
*C54	Luoh, et al., "Role of the Distal Half of the CMPL Intracellular Domain or Control of Platelet Production by Thrombopoietin in Vivo," <i>Mol. Cell. Biol.</i> , Vol. 20, No. 2, pp. 507-515 (2000)	
*C55	Landolfi, et al., "Aspirin in Polycythemia Vera and Essential Thrombocythemia: Current facts and Perspectives", <i>Leukemia and Lymphoma</i> , 1996, Vol. 22, Suppl. 1, pp. 83-86	

EXAMINER

DATE CONSIDERED

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/117,837, filed April 8, 2002, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]